Characterization Relevant to Personal Care Products

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Personal Care Products Council

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Technical Workshop Goal

- Council isn't a research institute but topic of great interest to personal care products industry
- Characterize & Exposure have been prominent on our agenda.
- This is due both to the essential role determining exposure plays in safety assessment but also because of the number of regulations which now include nano-specific obligations.
  - Europe Regulation (EC) No 1223/2009 labeling and premarket notification
  - Health Canada Sunscreen Record Keeping
- Share my learnings

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REPORTS* FOR ICCR

- Associations Survey of Nanomaterials Used in Cosmetic Products. October 2008 & June 2011
- Report of the Joint Regulator - Industry Ad Hoc Working Group:
  1. Currently Available Methods for Characterization of Nanomaterials; June 17, 2011
  2. Characterization of Nanomaterials II - Insolubility, Biopersistence and Size Measurement in Complex Media; July 2012
  3. Characterization of Nanomaterials III - Solubility, Stability & Persistence and Size Measurement in Complex Media; May 2013
- Report of the Joint Regulator - Industry Ad Hoc Working Group: Safety Approaches To Nanomaterials In Cosmetics; Nov 2013

* http://www.iccrnet.org/

International Cooperation on Cosmetics Regulation Initiative (ICCR)

- Est. 2007
- Voluntary group of cosmetics regulatory authorities working to remove regulatory obstacles among the regions, while maintaining the highest level of global consumer protection.
- Members:
  - Canada; European Union; Japan; United States; Brazil (2014);
  - Observers-China
- Nanomaterials on the first Agenda.

#1- 2008 Nanotechnology Inventory

- ICCR invited industry to:
  - develop common definitions for nanotechnology in the field of cosmetics; and
  - set up an inventory of current application of nano in this field.
  - Which would be used to determine the path forward
- Industry drafted number of key characteristics, relevant to cosmetics, as guidance
- Shared across all Associations members
- Reported basic survey out Aug. 2008 and expanded (product & frequency of use) in Oct. 2008

“Considerations”

- Stable & Insoluble
  - Excluding labile and soluble materials toxicokinetic view present no ‘exposure’
- Manufactured Intentionally
  - Excluding the universe of naturally occurring nanoscale materials ubiquitous in every day life
- “Nanometric” form
  - Including all types of nanomaterials (particles, aggregates, agglomerates, tubes/ rods)
- Size on the order of 1 to 100 nm
  - Recognition of the value of a uniform, if arbitrary, limits accept the more commonly referenced range

Questions & Concerns

- No surprising ingredients* but even with a simple inventory difficulties became evident.
- Didn't address many important questions- As example: Size
  - Different methods give different sizes
  - Agglomerates or aggregates
  - As Manufactured? As Sold? Final Formulation?
- Important to emphasis being listed wasn't in any way an implicit or explicit make conclusion on safety.
  - This is not a Risk Assessment
  - No Hazard Identification/ No Exposure Analysis

http://www.iccrnet.org/files/2814/3350/5427/2008-10_Association_Panel_Report_on_Nanotechnology_in_Cosmetics.pdf

2009 Joint Regulator- Industry JRC Workshop

- Following discussions at ICCR-2, European Joint Research Center with DG Enterprise organized *International Workshop on Regulatory Issues Regarding the Use of Nanotechnology in Cosmetics*, July 2009, at JRC in Ispra, Italy
  - Share current approaches & knowledge on nanomaterials in cosmetics, and to more thoroughly explore the challenges of regulating them.
- 28 experts from Gov'n & Industry: EC JRC, DG ENTR, R&I members from the 4 ICCR jurisdictions, the EU SCCS, the Nanotechnology Industry Association
- Following presentations of the state of science 2 break-out sessions
  - Definitions - Identification, Detection and Characterization
  - Regulatory Safety Testing.

Definitions Outcome

- Recognized that a complete characterization for scientific purposes, (hazard identification and risk assessment) is far more detailed than that needed within a regulatory framework.
- Agreed that for regulatory purposes simpler criteria, like those advanced within the ICCR framework would be sufficient.
- Characterization should be done on finished formulations but analysis methodology was probably not up to the task. Therefore rely on simplified models or on a raw materials basis.
- **Even so** additional work would be needed to fully clarify terminology like stable, insoluble, or 1 to 100 nanometers.

2010 Criteria and Methods of Detection

- Building on Ispra new work items proposed.
- Many organization active in area but ICCR, with its narrower focus on cosmetics, is in a strong position to establish criteria, that while consistent with international definitions is most relevant to cosmetics
- Joint Regulator- Industry Working Group established to recommend criteria determining if a material is considered “nanomaterial” within the 4 regions.

An insoluble ingredient, intentionally manufactured, with one or more dimensions in the realm of 1 to 100 nanometers in the final formulation and is sufficiently stable and persistent in biological media to allow for the *potential of interaction with biological systems*.

Analytical Methods

- Methods – 21 well developed, robust identified
  - 9 Spectroscopy; 3 Chromatography; 3 Microscopy & 6 Other Physical
- Parameters
  - Particles; Size & Distribution; Agglomeration/ Aggregation; Shape; Stability
  - Surface; Area, Chemistry, Charge
  - Chemical Composition

Most Relevant Methods by Parameter

		Spectroscopy									Chromato-graphy			Microscopy			Physical					
		AAS	DLS	LDE	ICP-MS	PALS	SAXS	XPS	XRD	XRF	CHDF	FFF	GE	SEM	SPM	TEM	AUC	BET	CPS	LD	SMPS	
Particle	Size & Distribution		X				X				X	X		X		X	X		X	X	X	X
	Agglomerate/ Aggregation		X				X							X	X	X				X	X	X
	Shape						X							X	X	X						
	Stability		X																			
Surface	Area																	X				
	Chemistry							X							X							
	Charge			X		X							X		X							
Chemical	Composition	X			X			X	X	X												

J. Ansell, D. Araki, et. al., "Report For International Cooperation On Cosmetic Regulation: Report of the Joint Regulator - Industry Ad Hoc Working Group: Currently Available Methods for Characterization of Nanomaterials, (2011)
http://www.iccrnet.org/files/9514/0475/4277/2011-06_Characterization_Approaches_to_Nanomaterials_in_Cosmetics.pdf

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Comparison Nano within a Regulatory Framework

EU Cosmetics Regulation	European Commission Recommendation 2011/696/EU	FDA
"nanomaterial" means an insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.	"Nanomaterial" means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm.	Whether an engineered material or end product has at least one dimension in the nanoscale range (approximately 1 nm to 100 nm); or exhibits properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer.

Critical Safety Parameters?

- ILSI – NanoCharacter Workshop Jan 2013
- Identified 28 separate lists (Govern; OECD; ECETOC; Individuals; Research Consortia)
  - 60 separate properties
  - Differencing terminology & by discipline
    - Inconsistent; cannot be measures in vivo; Qualitative - some not even be assigned units.

http://www.ilsi.org/NanoCharacter/Pages/NanoCharacter.aspx

Summary: Nanomaterials Characterization

- A number of well recognize methods are currently available to determine these parameters
- Various methods may have been used but may yield different results because they do not measure the same quantity
  - Size - primary particle, aggregated; agglomerate; hydrodynamic or aerodynamic
- No single method can, in and of itself, fully characterize
- Majority of methods require significant manipulation making properties under exposure conditions difficult to predict.
- Complicate in that none are ‘wrong’; they are ALL RIGHT

JRC Practical Challenges

- Regulation to Practice - Challenges
  - Measuring size of the constituent particle inside aggregates, agglomerates regardless of strength they are bound
  - Convert experimental measurements to number average distributions of polydisperse materials
  - Detect and count at sizes <10nm
- Currently usually not possible to determine primary particle unless the aggregates themselves meet the definition.
- Can only be used to show a material is a nanomaterial, NOT to show a material isn't.

AND THIS IS FOR PRISTINE SAMPLES

Challenges: Formulated Products

- Currently there is no method available to detect and characterize a nanomaterial directly complex environment.
- Simple act to isolate, observe, and quantify may change their physicochemical properties, making analysis extremely susceptible to artifacts.
  - The separation and/or extraction process itself can change the nanomaterial (aggregation, de-aggregation, etc.)
  - There is a lack of SOPs for sample preparation, and therefore reproducibility
  - Natural and engineered nanoparticles make it necessary to monitor of engineered nanoparticles within a huge background of unintentionally manufactured or natural nanoparticles.

JRC Take Aways

- Summarizing the current technical limitations , none of the currently available methods can determine for all kinds of potential nanomaterials whether they fulfill the definition or not.
- The determination of whether a product contains a nanomaterial, and eventually the quantity of the nanomaterials, is significantly more complex than just deciding whether a material fulfils the definition.

T. Lininger, G. Roebben, et.al., (2012) "JRC Reference Reports; Requirements on measurements for the implementation of the European Commission definition of the term "Nanomaterial", EUR 25404 EN

In Summary

- Many methods require significant sample preparation and so may have little bearing on the nanostructure as used.
- Must avoid having scientifically precise reports wholly divorced from the conditions relevant to exposure.
- A material that may be nanostructured may be considered a nanomaterial based on one set of definitions, but, in fact, have no nanoparticles under actual conditions of use.
- Great care in reporting and interpretation of results to avoid confusion with characterization for regulatory purposes and assessing the safety of nanomaterials.